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1637	19

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/450,651	ANDERSSON ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *9,12,13 and 42-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,11,14-41 and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (Methods of breed determination ***using a nucleic acid***, encompassing claims 1-8, 10, 11, 14-41, and 48-50, and the election of coat color gene, and the polymorphism at position 60) in Paper No. 17, filed on June 11th, 2002 is acknowledged.

It is noted that the claims must be amended to clearly recite the elected invention.

Priority

2. It is noted that only claims relating to the α MSHR gene and polymorphisms disclosed therein, i.e., claims 10, 16, 20, 34 and 48 have priority to Great Britain Application No. 9711214.8, filed on May 30, 1997.

Claims directed to the KIT gene and methods for analyzing breed determinant genes, i.e., claims 1-8, 11, 14-15, 17-19, 21- 23, 29-33, 36-41 and 49-50 have priority to Great Britain Application No. 9801990.4, filed on January 31, 1998. It is noted that a claim that has priority, in part, to two different applications will receive the priority of the later application.

Finally, claims directed to determining the Belt genotype from the Kit gene, i.e., claims 24-28, and claims directed to the specific polymorphism at position 60 of the α MSHR gene, i.e., claim 35 have priority to PCT/GB98/01531, filed on May 27, 1998.

Sequence Notes

3. This application fails to comply with the requirements of 37 C.F.R. 1.821(d), as Claim 37 does not provide the appropriate SEQ ID NOS: for nucleic acid sequences. Claim 37 should be amended to insert the appropriate sequence identifying (SEQ ID NO) following each recited sequence. Furthermore, on page 64, Applicants should amend the specification to include the appropriate SEQ ID NOS. See MPEP Chapter 2400.

Information Disclosure Statement

4. The information disclosure statement of Paper No. 4, filed on April 10, 2000 complies with CFR 1.97, 1.98, and M.P.E.P. 609, and has been considered (see enclosed signed PTO-1449).

Specification

5. The disclosure is objected to because of the following informalities:

A) On page 25 the specification should recite 1A and 1B when describing Figure 1.

B) The claims should be amended to only recite the elected invention (e.g., coat color gene and the polymorphism at position 60) (specifically with respect to claims 6-7, 14, 17-19, 21-25, 29-33, 35-38.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-8, 10, 11, 14-41 and 48-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 10, 20 and 26 because the claims do not recite a final process step, which clearly relates back to the preamble. For example (with respect to claims 10, 20 and 26), it is not clear whether the method is drawn to determining the coat color genotype of a pig or to analyze a nucleic acid. In addition, the claims are indefinite as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. For example, it is unclear as to how one validates an animal product by simply obtaining a sample of an animal product and analyzing an allele of a breed determinant gene present in said sample.

B) Claim 1 over "the allele(s)" because these recitations lack antecedent basis. That is, it is not clear as to whether this refers to a specific allele, all the alleles (i.e., at every possible position), or any combination of alleles.

C) Claims 2-4 over "the breed determinant" because this recitation lacks antecedent basis. That is, it is not clear as to whether this is an overt phenotypic trait or some other trait. The specification (pg. 4, ln. 1-2) teaches that a breed determinant is used to "indicate an overt phenotypic characteristic", however, the claims depend from claim 1, which states, "analyzing the allele(s) of one or more breed determinant *genes*".

D) Claim 15 because it is not clear how one "establish[es] the presence or absence of at least one nucleotide change" or "identifying the presence or absence of at least one missense mutation" when the claim does not specify a comparison to a normal KIT or αMSHR gene to determine whether there is in fact a presence or absence of a nucleotide change.

F) Claims 17 and 19-20 over "or other linked marker alleles" because it is not clear as to what "other linked marker alleles" are linked to the KIT or αMSHR gene. Does this term refer to linkage disequalibrium or to any gene in any way associated with the KIT or αMSHR gene (i.e., on a different chromosome)? How many "other linked marker alleles" are possible? How does one determine another "linked" marker allele?

G) Claim 20 is also indefinite because it is not clear as to what "particular alleles of the αMSHR gene" are being referred too. That is, it is not clear as to how one determines the association between one or more microsatellite or other linked marker alleles and "particular alleles of the αMSHR gene". Applicants should clearly refer to what alleles are considered to be "particular alleles of the αMSHR gene".

H) Claims 30-31 over "breed specific marker" because it is not clear as to what encompasses a "breed specific marker". That is, how is a breed "specific" marker different from a breed marker. On page 4, the specification states, "breed marker...is used herein to define other characteristics which appear to be breed specific on the basis of empirical data". It is not clear as to what "other characteristics" are being referred to, in addition to a lack of information as to what empirical data is being considered, and what outcomes are necessary to determine when data meets the criteria of "breed specific".

I) Claims 32, 36 and 38 over "suitable primers" because it is not clear as to what primers are considered to be "suitable". Are suitable primers a certain length, do they only amplify a particular region or do they amplify the entire gene?

Claim Rejections - 35 USC § 112, 1st Paragraph – Written Description

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-8, 10, 11, 14-41 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to:

1) differentiating animals and animal products on the basis of breed origin; or

2) determining or testing the breed origin of an animal product; or

3) validating an animal product;

comprising the steps of:

(i) providing a sample from ***any*** animal product, and

(ii) analyzing ***any*** allele(s) of ***any*** one or more breed determinant genes present in the sample.

4) determining the coat color genotype of a pig comprising the steps of,

(i) obtaining a sample of pig nucleic acid; and

(ii) analyzing the nucleic acid obtained in (i) to determine if ***any*** allele(s) of the αMSHR gene are present, wherein the presence or absence of an allele would be indicative of coat color genotype.

5) determining the coat color genotype of a pig comprising the steps of,

(i) determining the association between ***any*** one or more microsatellite or ***any*** other linked marker alleles linked to the αMSHR gene and particular alleles of the αMSHR gene;

(ii) obtaining a sample of pig nucleic acid; and

(iii) analyzing the nucleic acid obtained in (ii) to determine if ***any*** microsatellite or other linked markers alleles are present.

6) determining the coat color genotype of a pig comprising the steps of,

(i) obtaining a sample of pig nucleic acid; and

(ii) analyzing the nucleic acid obtained in (i) to determine whether the KIT gene carries ***any*** polymorphism associated with Belt genotype.

These claims encompass an extremely large genus of polymorphisms correlated to any phenotype from any animal. However, the specification has only taught:

- a 2 bp insertion in the αMSHR gene of Pietrain and Large White pigs;
- a polymorphism at position 1162 of αMSHR gene, which is unique to the European Wild Boar, wherein the European Wild Boar has an A at this position, as opposed to 5 other breeds, which have a G;
- a polymorphism at position 941 of the bovine myostatin gene, wherein a G at position 941 of the Belgian Blue and Holstein-Friesian breeds led to the double muscle phenotype, whereas the Piedmontese breed had an A at position 941, and was normal;
- a substitution of the G of the conserved GT pair with A at the exon17/intron17 splice site of KIT2 (i.e., nucleotide position 1 of intron 17) in the second copy of

KIT gene that results in a single splice variant KIT protein lacking exon 17 and results in a pig with white coat color; and

- an unidentified polymorphism and a polymorphism at position 2678 of the KIT gene which creates the Belt phenotype in Hampshire pigs.

The correlations between these specific polymorphisms in specific genes, and their respective phenotypes or breed determinants are not a representative sample of the large number of polymorphisms and correlated phenotypes or breed determinants encompassed by the claims. In addition, these polymorphisms encompass changes in undisclosed nucleic sequences, and nucleic acid sequences which are not described.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention. The invention is, for purposes of the written description inquiry, *whatever is now claimed* (See page 1117)." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (See Vas-Cath at page 1116)."

The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's

were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Accordingly, absent a teaching of a representative number of polymorphisms correlated to the large number of possible any phenotypes or breed determinants, the specification provides insufficient written description to support the broadly claimed genus.

Claim Rejections - 35 USC § 112, 1st Paragraph – Enablement

10. Claims 1-8, 10, 11, 14-41 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient

evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (see *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

Nature of the Invention
Amount of Direction or Guidance Presented
Presence and Absence of Working Examples
Quantity of Experimentation Necessary
Level of Predictability and Unpredictability in the Art

I. ***NATURE OF THE INVENTION***

A) The invention is directed to methods of:

1) differentiating animals and animal products on the basis of breed origin; or

2) determining or testing the breed origin of an animal product; or

3) validating an animal product;

comprising the steps of:

(i) providing a sample from ***any*** animal product, and

(ii) analyzing ***any*** allele(s) of ***any*** one or more breed determinant genes present in the sample.

The specification teaches an animal product could encompass foodstuffs, semen or other products for use in breeding programs (see pg. 6, ln. 12-13). The specification also states, "breed determinant gene is used to indicate a gene which is involved (at least in part) in the expression of the corresponding overt phenotypic characteristic." (pg. 4, ln. 6-8). Therefore, a breed determinant gene could encompass even a gene that is only partly involved in expression. Accordingly, the claims are broadly drawn to include analyzing ***any*** possible allele of ***any*** breed

determinant gene (which could only be partly involved in gene expression) from ***any*** animal product (e.g., other than pig or cattle).

4) determining the coat color genotype of a pig comprising the steps of,

(i) obtaining a sample of pig nucleic acid; and

(ii) analyzing the nucleic acid obtained in (i) to determine if ***any*** allele(s) of the αMSHR gene are present, wherein the presence or absence of an allele would be indicative of coat color genotype.

That is, the claims encompass analyzing ***any*** allele(s) found throughout the entire αMSHR gene, and determining whether ***any*** allele(s) is/are involved in coat color genotype of a pig.

5) determining the coat color genotype of a pig comprising the steps of,

(i) determining the association between ***any*** one or more microsatellite or ***any*** other linked marker alleles linked to the αMSHR gene and particular alleles of the αMSHR gene;

(ii) obtaining a sample of pig nucleic acid; and

(iii) analyzing the nucleic acid obtained in (ii) to determine if ***any*** microsatellite or other linked markers alleles are present.

That is, the claims encompass analyzing the association of ***any*** microsatellite or other linked marker allele "linked" to the αMSHR gene, and determining whether ***any*** microsatellite or other linked marker allele "linked" to the αMSHR gene is involved in coat color genotype of a pig.

6) determining the coat color genotype of a pig comprising the steps of,

(i) obtaining a sample of pig nucleic acid; and

(ii) analyzing the nucleic acid obtained in (i) to determine whether the KIT gene carries ***any*** polymorphism associated with Belt genotype.

That is, the claims encompass analyzing the association of ***any*** polymorphism in the entire KIT gene (i.e., at any possible position of the KIT gene), and determining whether ***any*** polymorphism in the KIT gene is associated with Belt genotype.

II. *PRESENCE AND ABSENCE OF WORKING EXAMPLES & AMOUNT OF DIRECTION AND GUIDANCE*

The specification teaches:

Example 2 (pgs. 30-34) teaches PCR-RFLP based discrimination of alleles at the *E* locus of the αMSHR gene. Specifically, the example teaches *E* genotypes for a range of pig breeds using the *Bst*UI/*Hha*I digestion system.

However, Example 2 does not teach an association between ***any*** genotype with ***any*** polymorphism of ***any*** animal. Furthermore, the specification provides no universal correlation between ***any*** polymorphism at ***any*** position of the αMSHR gene, and whether a specific breed of pig would be associated with a polymorphism at any position. It is also noted that neither the full-length sequence of the αMSHR gene nor a complete ORF are disclosed, instead Example 1 illustrates that only a partial coding sequence is disclosed by the specification (pg. 30, see Results). While Example 2 teaches that Large White, Landrace, Pietrain and Berkshire breeds all had same genotype, as well as, Bazna and Meishan breeds having the same genotype (pg. 33), the specification does not teach how the skilled artisan would use this information to determine

coat color phenotype, or any other phenotype or breed determinant of any animal. Further experimentation would be required of the skilled artisan to determine a use for the genotype show in Example 2.

Example 7 (pg. 39) teaches the discrimination of cattle products by breed, wherein in Bovine myostatin, the following polymorphisms led to the following phenotype at nucleotide position 941.

Breed	Phenotype	nt position 941	Length of PCR product (bp)
Belgian Blue	Double Muscle	G	482
Piedmontese	Normal	A	493
Holstein-Friesian	Double Muscle	G	493

However, it is not clear as to whether position 941 refers to the full length bovine myostatin gene, an ORF, or a PCR product thereof. Additionally, Example 7 does not teach an association betweena ***any*** genotype or breed determinant with ***any*** polymorphism of the bovin myostatin gene of ***any*** animal. Furthermore, the specification provides no universal correlation between ***any*** polymorphism at ***any*** position of the Bovine myostatin gene, and whether a specific breed of cattle or any other animal would be associated with a polymorphism at any position. Finally, there is no teaching in the specification as to how the information in this example would be used by one of skill in the art, without further experimentation. For example, on page 7, the specification discusses mutations in the bovine myostatin gene, wherein the Belgian Blue and Asturiana breeds' contain an 11 bp deletion, whereas in the Piedmontese breed a G to A transition is present. Thus, the specification asserts that polymorphism detection of the bovine myostatin gene is not only highly unpredictable from breed to breed, but does not provide

guidance to one skilled in the art as to how to use information regarding polymorphisms associated to the bovine myostatin gene. Furthermore, Grobert et al. (Nature Genetics (1997) 17(1): 71-74) teaches:

> The identification of the MSTN as the gene causing the double-muscled genotype will allow for the development of diagnostic tests that will facilitate the selection for or against this trait in cattle...It would be interesting to determine whether inactivation of MSTN...might still lead to an increased muscle development. Moreover, the identification of the myostatin gene as a key regulator of muscle development will permit study of upstream and downstream factors...that might lead to the identification of other genes underlying genetic variation for muscle development in livestock.

(pg. 74, 1st column). Therefore, Grobert does not overcome the deficiencies in the specification, since he teaches that associating polymorphisms in the bovine myostatin gene is only a starting point for identifying other genes and further testing.

Examples 8 (pgs. 40-41) teaches that Exon 17 was missing from a 301 bp truncated cDNA fragment from Large White pigs, as compared to a 424 bp fragment in Hampshire pigs, when a 424 bp fragment including KIT cDNA exon 16-19 was amplified from both Hampshire and Large White pigs. Examples 9-13 (pgs. 41-52) teach a method for determining whether a pig has a white coat color, comprising obtaining a sample of pig nucleic and analyzing the nucleic acid obtained to determine whether a substitution of the G of the conserved GT pair with A at the exon17/intron17 splice site of KIT2 (i.e., nucleotide position 1 of intron 17), wherein presence of said substitution is correlated with coat color.

However, Examples 8-13 do not teach an association between ***any*** genotype with ***any*** polymorphism in the KIT gene of ***any*** animal. Furthermore, the specification provides no universal correlation between ***any*** polymorphism at ***any*** position of the KIT gene, and whether a coat color of a pig would be associated with a polymorphism at any position. Additionally, the

specification does not teach correlating coat color to any of the various substitutions, insertions, deletions or frame shift mutations in exons or introns of the KIT gene that are encompassed by the claims. Further, the specification, provides no guidance as to the effect the myriad, of the large genus, of mutations encompassed by the claims, that could occur in the KIT gene, would have on the KIT mRNA or protein, nor how this would affect the coat color of a pig. Additionally, the specification does not teach what the coat color of a pig would be if only a single copy of the KIT gene is present and possesses the G to A substitution in the conserved GT pair.

Example 14 (pgs. 52-55) teaches of an unidentified polymorphism of the KIT gene (i.e., it is not clear as to what polymorphism is being referred to, e.g., the position of the polymorphism does not appear in the Example), which appears to be closely associated with the dominant white phenotype. Additionally, Example 14 does not teach an association between ***any*** genotype with ***any*** polymorphism in the KIT gene, in ***any*** animal. Furthermore, the specification provides no universal correlation between ***any*** polymorphism at ***any*** position of the KIT gene, and whether a specific breed of pig would be associated with a polymorphism at any specific position. Additionally, it is unclear how the skilled artisan would use this polymorphism because the specification teaches that; "it is not completely associated with the [KIT] duplication as some white animals did not show the heteroduplex pattern." (pg. 55). Further experimentation would be required of the skilled artisan to determine a use for the unidentified polymorphism taught in example 14 of the specification.

Example 19 (pgs. 64-66) teaches that nucleotide position 2678 of the KIT gene is polymorphic, wherein a C or T occurs at this position. The presence of a C creates a restriction

site for *Aci*I, and thus, a heterozygous genotype (i.e., C/T) at position 2678 in the KIT gene creates the Belt phenotype in Hampshire pigs.

Firstly, example 19 does not teach how one of skill in the art would use the association between the polymorphism taught in example 19 and the Belt phenotype in Hampshire pigs. In other words, the specification does not teach why determining that a pig has the Belt phenotype would be useful. Further, even if the skilled artisan would know how to use the association between the 2678 polymorphism, Example 19 does not teach an association between ***any*** polymorphism in the KIT gene and ***any*** phenotype or breed determinant, in ***any*** animal (e.g., cow). Furthermore, the specification provides no universal correlation between ***any*** polymorphism at ***any*** position of the KIT gene, and whether a specific breed of pig would be polymorphic at any position of the KIT gene. Additionally, the specification has not demonstrated whether the C/T genotype at position 2678, in other organisms (e.g., cow or even other breeds of pigs), would have the same function or correlation as it does in the Hampshire pig.

Examples 20-21 (pgs. 66-70) teach that a 2 bp insertion in the αMSHR gene of a Pietrain and Large White breeds creates a TGA stop codon. This 2 bp insertion was only identified in Pietrain and Large White pigs, two breeds ascribed to the E^P alleles, but not in the Hampshire breed, which carries E^H. Example 22 (pgs. 70-71) teaches a polymorphism at position 1162 in the αMSHR gene, which is unique to the European Wild Boar. The European Wild Boar has an A at this position, as opposed to 5 other breeds, which have a G.

However, Examples 20-22 do not teach an association between ***any*** genotype with ***any***

polymorphism of ***any*** animal. Furthermore, the specification provides no universal correlation between ***any*** polymorphism at ***any*** position of the αMSHR gene, and whether a specific breed of pig would be associated with a polymorphism at any position. Additionally, it is unclear how the skilled artisan would use either polymorphism, as the specification has not correlated these polymorphisms with any specific phenotype or breed determinant.

III. ***LEVEL OF PREDICTABILITY AND UNPREDICTABILITY IN THE ART***

The art does not teach of a correlation between any possible mutation in the αMSHR, the bovine myostatin gene, the KIT gene and coat color, or any phenotype or breed determinant of a pig or any animal. Since it is unclear from the teachings in the specification or the art as to how mutations in the αMSHR, bovine myostatin, or KIT gene affect coat color in a pig (or any other phenotype or breed determinant encompassed by the claims), it is unpredictable as to whether the myriad of mutations in either one or a second or both copies of the αMSHR and/or KIT gene, or the bovine myostatin gene encompassed by the broadly claimed invention would affect coat color in a pig, or any phenotype or breed determinant in any animal, or how they would affect any phenotype or breed determinant in any animal. The claims encompass an extremely broad number of possible correlations between polymorphisms in any gene and any phenotype or breed determinant in animal, however neither the specification nor the art teach a predictable correlation between the large number of possible mutations in the single αMSHR, or bovine myostatin, or KIT gene, and any phenotype or breed determinant in any animal to enable the full scope of the broadly claimed invention.

With respect to the αMSHR gene, the specification teaches varying alleles at the *E* locus, a 2 bp insertion in Pietrain and Large White pig, two breeds ascribed to the E^P alleles, but not in the Hampshire breed, which carries E^H, and a polymorphism at position 1162, which is unique to the European Wild Boar, wherein the European Wild Boar has an A at this position, as opposed to 5 other breeds, which have a G. However, it is unclear as to how the varying alleles, 2 bp insertion and polymorphism at position 1162, affects the structure and function of the αMSHR gene or the protein encoded by the αMSHR gene, and how any of these mutations are associated with any breed determinant. Furthermore, the specification has not taught any universal correlation between polymorphisms in the αMSHR gene and any specific phenotype or breed determinant in any animal. Without this information the skilled artisan would not be able to predict which substitutions, additions, deletions or frameshift mutations in the αMSHR gene would result in a particular phenotype or breed determinant.

With respect to claim 35 and the elected polymorphism at position 60, neither the specification nor the art teach either the presence of a polymorphic nucleotide or site at this position, or whether a polymorphic nucleotide or site would be correlated with coat color in a pig. Neither the specification nor the art have taught how coat color is affected by polymorphisms in the αMSHR gene in pigs (e.g., function of the encoded protein), or that a universal correlation exists between any polymorphisms in the αMSHR gene and coat color. Accordingly, absent such evidence, the skilled artisan would be unable to predictably correlate whether a polymorphism at position 60 of the αMSHR gene (or any position) would be associated with coat color, without further and undue experimentation.

With respect to the bovine myostatin gene, the specification teaches that a G at position 941 of the Belgian Blue and Holstein-Friesian breeds led to the double muscle phenotype, whereas the Piedmontese breed had an A at position 941, and was normal. However, it is unclear as to how the polymorphism at position 941, affects the structure and function of the bovine myostatin gene or the protein encoded by the bovine myostatin gene, and how this mutation is associated with double muscling. Furthermore, the specification has not taught any universal correlation between polymorphisms in the bovine myostatin gene and double muscling in cattle. Without this information the skilled artisan would not be able to predict which substitutions, additions, deletions or frameshift mutations in the bovine myostatin gene would result in double muscling. Moreover, as discussed above, the specification and the prior art of Grobert teach that associating polymorphisms in the bovine myostatin gene is only a starting point for identifying other genes and further testing. Accordingly, not only are finding polymorphisms in the bovine myostatin gene that are associated with double muscling unpredictable, absent guidance in the specification, but even if polymorphisms are determined, they provide, at best, only a starting point for further research.

With respect to the KIT gene, the specification teaches a substitution of the G of the conserved GT pair with A at the exon17/intron17 splice site of KIT2 (i.e., nucleotide position 1 of intron 17), an unidentified polymorphism and a polymorphism at position 2678 which creates the Belt phenotype in Hampshire pigs. However, it is unclear as to how the known and unknown polymorphisms, affects the structure and function of the KIT gene or the protein encoded by the KIT gene, and how any of these mutations are association with coat color or the Belt phenotype. Furthermore, the specification has not taught any universal polymorphisms in the KIT gene,

which are associated with coat color or the Belt phenotype. Without this information the skilled artisan would not be able to predict which substitutions, additions, deletions or frameshift mutations in the KIT gene would result in a particular coat color phenotype or the Belt phenotype.

Additionally, neither the specification nor the art teach a predictable correlation between the extremely large numbers of possible alleles of one or more breed determinant genes present in any animal product. The specification only teaches of a single substitution from a G to an A in the conserved GT pair at the exon17/intron17 splice site (nucleotide position 1 of intron 17) in the second copy of KIT gene that results in a single splice variant KIT protein lacking exon 17 and results in a pig with white coat color.

The porcine KIT gene contains at least 19 exons. Splice variant proteins encompassed by the claims include variants lacking single or multiple exons or parts of exons of the KIT protein, however, the specification has not provided any guidance as to the effect that the large number of splice variants encompassed by the claim, would have on the coat color of a pig. The single mutation which leads to the single splice variant protein lacking exon 17 taught by the specification is not sufficient to establish a predictable correlation for the skilled artisan between the large number of mutations that might result in an altered exon 17 (not necessarily completely excised, as discussed by the specification at page 4) or splice variant proteins encompassed by the claims and white coat color of a pig. Further, the specification provides no guidance as to how the splice variant protein lacking exon 17 leads to white coat color in a pig, such that the skilled artisan might be able to establish a predictable correlation between the effect the lack of exon 17 has on the function of the porcine KIT protein and other splice variants of the porcine

KIT protein. As correlating a particular coat color with the large number of mutations in the KIT gene encompassed by the broadly claimed invention is unpredictable in light of the lack of teaching and guidance in the specification and the art, the skilled artisan would be required to perform undue experimentation to make or use the invention as broadly as it is claimed. While the amount of experimentation needed is not necessarily considered undue, such experimentation would be replete with trial and error, thus constituting undue experimentation.

Moreover, the specification states, "as with porcine coat color a single selected characteristic is caused by a number of potential polymorphisms" (pg. 7, ln. 19-20). Therefore, the specification asserts that any particular phonotype could be affected by more than one polymorphism in a single gene or multiple genes. However, neither the specification nor the art enable the skilled artisan to predictably determine what the identity of these polymorphisms are, without further undue experimentation.

IV. ***THE QUANTITY OF EXPERIMENTATION NECESSARY***

With respect to methods 1-3 detailed above in order to practice the invention, the practitioner would be required to obtain different types of animal product from an extremely large number of different species, and analyze said product for ***any*** allele(s) of ***any*** one or more breed determinant genes, and then correlate the presence or absence of the allele(s) to differentiate, determine or test the animal's breed origin, or validate the animal product. This minimally involves, at least, obtaining animal products (from any animal), such as foodstuffs, semen or other products for use in breeding programs, screening the animal product's complete DNA for any allele(s) and/or polymorphisms in any one of a large plurality of possible breed determinant genes (those which may only partly be involved in gene expression), and then

attempt to correlate these alleles with breed origin, for example. This could encompass creating a database comprising all the allele(s) and/or polymorphisms associated with breed determinant genes in any animal and their corresponding origins. Such experimentation requires an extremely large amount of trial and error analysis, with little to no starting point, wherein the results of such analysis are unpredictable, and is therefore considered undue

With respect to method 4 detailed above in order to practice the invention, the practitioner must perform experiments testing ***every possible*** allele at ***every possible position*** of the αMSHR gene, and attempt to correlate said allele to coat color or [any breed determinant] in pigs. Due to the size of the αMSHR gene, the full sequence of which the specification does not disclose, this could amount to millions or more possible permutations. This experimentation would be completely driven by a trial and error process with no guidance from either the specification or the art. Accordingly, because the skilled artisan must supply novel experimentation of first finding and then correlating alleles of the αMSHR gene and coat color, the experimentation is considered undue.

With respect to method 5 detailed above in order to practice the invention, the practitioner must perform experiments testing ***every possible*** microsatellite or other linked marker alleles linked to the αMSHR gene, and attempt to correlate said microsatellite or other linked marker alleles linked to the αMSHR gene to coat color in pigs. This experimentation would be completely driven by a trial and error process with no guidance from either the specification or the art, the results of which are unpredictable. Accordingly, because the skilled artisan must supply novel experimentation of finding and correlating microsatellite or other

linked marker alleles linked to the αMSHR gene and coat color, the experimentation is considered undue.

With respect to method 6 detailed above in order to practice the invention, the practitioner must perform experiments testing ***every possible*** polymorphism at ***every possible position*** of the KIT gene, and attempt to correlate said polymorphism with the Belt genotype, and then correlate said polymorphisms associated with said Belt genotype to coat color in pigs. Due to the size of the KIT gene, this could amount to millions or more possible permutations. This experimentation would be completely driven by a trial and error process with no guidance from either the specification or the art as to which polymorphisms would be predictably correlation. Accordingly, because the skilled artisan must supply novel experimentation of finding and correlating polymorphism of the KIT gene, Belt genotype and coat color, the results of such analysis being unpredictable, the experimentation is considered undue.

Accordingly, in view of the unpredictability in the art and in view of the lack of specific disclosure in the specification, undue experimentation would be required to practice the invention as it is claimed.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-8, 11, 14-15, 17, 19-22, 29-30, 32, 39-41 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Kriegesmann et al. (WO 96/34982).

Kriegesmann teaches methods of analyzing alleles in the MSHR gene (see abstract and pgs. 2-7). Specifically, Kriegesmann teaches providing a sample of an animal product (e.g., semen), and analyzing the alleles of the αMSHR (i.e., breed determinant) gene (pg. 2, ln. 28-33 and pgs. 4-7) (claims 1, 7, 8, 11, 21-22, 29-30, 39-41 and 50). Kriegesmann teaches the breed determinant is coat color (i.e., coat color locus), which is an overt phenotypic trait (e.g., behavioral or morphological) and varies qualitatively or quantitatively between breeds (pgs. 1-3 and 7) (claims 2-6). Kriegesmann teaches analyzing the alleles of cattle using PCR using specific primers and methods of detection (e.g., using probes, SSCP, etc.). (pgs. 3, ln. 19 to pg. 7, ln. 10 and pgs. 9-10) (claims 14-15, 17, 19-20 and 32).

It is noted claims 17 and 19-20 are included in this rejection in view of the lack of clarity of the recitation of "other linked marker alleles".

13. Claims 1-8, 11, 14-17, 19, 21-23, 29-30, 32, 39-41 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Moller et al. (Mammalian Genome (1996) 7: 822-830).

Moller teaches providing a DNA sample from a pig, and analyzing the allele(s) of the KIT gene (i.e., breed determinant coat color gene) from said sample (see abstract and pgs. 822-823, 825 and 827-829) (claims 1-8, 11, 19, 21-23, 29-30, 32, 39-41 and 50). Moller also teaches determining the sequence of the KIT gene (pg. 823) (claim 14). Moller also teaches mutation detection analysis, wherein some KIT polymorphisms are associated with coat color in pig (pg. 825) (claims 15-17).

It is noted claims 17 and 19 are included in this rejection in view of the lack of clarity of the recitation of "other linked marker alleles".

14. Claims 1-5, 8, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Grobert et al. (Nature Genetics (1997) 17(1): 71-74).

Grobert teaches providing a DNA sample from a cow, and analyzing the allele(s) of the Bovine myostatin gene (i.e., breed determinant gene) from said sample (see abstract and pgs. 71-73) (claims 1-5 and 8). Grobert teaches performing PCR on a specific fragment of the bovine myostatin gene (pg. 74, 2nd column) (claim 11).

15. Claims 1-8, 11, 14-17, 19, 21-23, 29-30, 32, 39-41 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Marklund et al. (Mammalian Genome (1996) 7(12): 895-899).

Marklund teaches providing a DNA sample from a horse, and analyzing the allele(s) of the αMSHR gene (i.e., breed determinant coat color gene) from said sample (see abstract and pgs. 895-896) (claims 1-8, 11, 19, 21-23, 29-30, 32, 39-41 and 50). Moller also teaches determining the sequence of the αMSHR gene (pg. 896) (claim 14). Moller also teaches mutation detection analysis, wherein some αMSHR polymorphisms are associated with coat color in pig (pg. 896-898) (claims 15-17).

16. Claims 1-8, 11, 14-15, 17-19, 21-23, 29-33, 36-41 and 49-50 provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/550,605, which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application it would constitute prior art under 35 U.S.C. 102(e), if published

under 35 U.S.C. 122(b) or patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future publication or patenting of the copending application.

Copending application No. 09/550,605 teaches method for determining whether a pig has a white coat color, comprising obtaining a sample of pig nucleic and analyzing the nucleic acid obtained to determine whether a substitution of the G of the conserved GT pair with A at the exon17/intron17 splice site of KIT2 (i.e., nucleotide position 1 of intron 17), wherein presence of said substitution is correlated with coat color.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-8, 11, 14-15, 17-19, 21-23, 29-33, 36-41 and 49-50 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-13, 18-19 of copending Application No. 09/550,605. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims 1, 4-13, and 18-19 of the '605 application are a species of the genus claimed in the instant application. Accordingly, because '605 claims a species of the genus instantly claimed, the claims are coextensive in scope and are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. No claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Souaya, can be reached at (703) 308-6565. If attempts to reach Jehanne Souaya are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or

proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
July 10, 2003

JEHANNE SOUAYA
~~PATENT~~ EXAMINER
Primary
July 11, 2003